Health Effects of Pesticides

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Why Talk About Pesticide Toxicity?

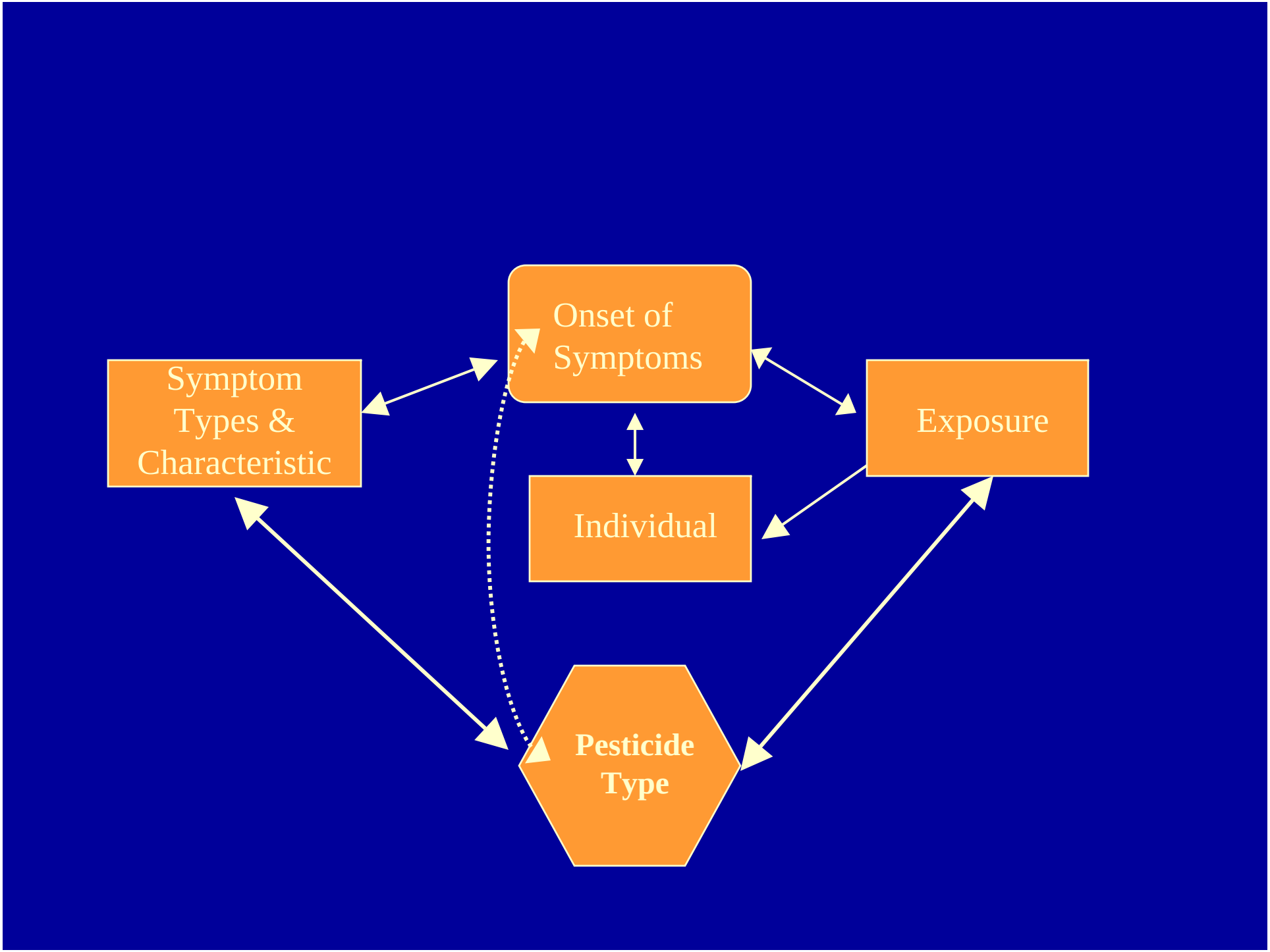
- Evaluate effects of pesticides according to routes of exposure
- Have a general understanding of pesticide effects to generate questions to ask during a pesticide illness or injury
- Use expertise on pesticide uses as it relates to its toxicity

How is Information Collected?

- DFROII or PIR
- Interviews
- Medical Records

What Information is Necessary for Documentation?

- Onset of Symptoms
- Types and Characteristic of Symptoms
- Type of Exposure
- Type of Pesticide


Onset of Symptoms
Symptom Types & Characteristic
Exposure
Individual
Pesticide Type

Onset of Symptoms

- Necessary to evaluate relationship of exposure to illness
- Necessary to evaluate pesticide effects to exposure
- Example:
  - Fieldworker developed skin irritation 3 weeks after working in a field sprayed with benomyl.
  - Fieldworker developed skin irritation 1 day after working in a field sprayed with benomyl.

Non-Specific Symptoms and Signs

- Rash
- Flu-like symptoms
  - Dizziness, malaise, respiratory tract irritation
- Gastrointestinal symptoms
- Seizures
- Odor-related effects
  - Not toxicological effects of active ingredient

Pesticide Illness May Mimic Common Medical Conditions

- Mild:
  - Upper respiratory tract infection/influenza
  - Food-borne illness
  - Asthma
  - Plant-induced irritant or allergic dermatitis
- Severe:
  - Cerebrovascular accident
  - Psychiatric dysfunction
  - Heat stroke

Symptom Characteristics

- Allergic
  - Symptoms seen in predisposed individuals who have a history of being allergic to chemicals
  - Most of this information is from the individual or from the doctor who knows of the patient's history

Toxicity of Pesticides

- Pesticides range in toxicity from virtually harmless to extremely toxic
- Some are among the most toxic products produced by man

Toxicity of Pesticides

- There are both acute and chronic toxicities associated with pesticides
- Health effects may be due to any component of pesticide formulations
- Some effects are as yet unexplored

Pesticides Since WWII

- Through the 60-70s Ops and Carbamates predominated among insecticides
- Pyrethrins strong but resistance a problem
- Herbicides
  - The deregistration of 2,4,5-T eliminated the issues of dioxin in herbicides
  - Paraquat remains highly toxic and widely used

Pesticides Since WWII

- Fungicides
  - The main issues are carcinogenicity and a question of metalotoxicity
- Fumigants: Standard group with little change

Pesticide Groups

- Fungicides
- Herbicides
- Insecticides
- Others

Fungicides

- Acute Effects
  - Irritant & allergic dermatitis
- Chronic Effects
  - Chronic dermatitis
  - Possible carcinogens

Fungicides: Thiocarbamates

- Related chemicals,Thiram, Maneb and Zineb
  - Sensitization reported in exposed workers
    - 1990, 26 cases of dermatitis among pear harvesters in Washington state, entered field 5 days after application.
    - Residue data from manufacturer stated a 9-day half-life for the chemical
    - Reentry interval increased to 14 days
  - "Antabuse" effects especially when alcohol ingested after exposure

Fungicides: Thiocarbamate reactions

Antabuse effect- experience severe flushing reactions with headache, nausea and vomiting if alcohol is ingested shortly after exposure.

Fungicides: Chlorothalonil

- Itching and hives in redwood nursery worker
- Chlorothalonil patch test:
  - Local Type I hypersensitivity
- 1% chlorothalonil open test
  - Systemic Type I reaction

Fungicides: Chlorothalonil

- Pigmentary Changes
  - Blue-gray pigmentation in
  - antecubital area
  - Positive skin reaction
  - to chlorothalonil
  - Diagnosis: Ashy dermatitis

Fungicides: Chlorothalonil

- Ashy dermatitis

Fungicides: Sulfur

- Potent skin irritant
  - Animal experiments equivocal
- Airway irritant

Fungicides: Sulfur

Positive patch test reaction to a sulfur. This was a subject in a study of nursery workers in California. Positive reactions support sulfur-induced allergy.

Fungicides: Sulfur

Apparent irritation reaction to a sulfur-malathion mixture plus a sweaty forearm

Fungicides: Benomyl

- Studies have shown benomyl to be a potent experimental allergen

- Several cases in a nursery implicated benomyl to cause an allergic contact dermatitis

Herbicides

- Dipyridyl compounds
  - Paraquat
  - Diquat
- Glyphosate
- Phenoxy compounds
  - 2,4,5T (2,4,5-T)
  - 2,4 (2,4-D)

Herbicides: Dipyridyl Compounds

- Paraquat - Gramoxone™
- Diquat - Actor ™

- Extremely toxic via ingestion
  - LD_{50} 3-5 mg/kg
- Toxicity
  - Skin, pulmonary
  - Parkinson's Disease?

Herbicides: Dipyridyl Compounds

Botella et al, 1985

Hoffer and Teitelman, 1989

Herbicides: Paraquat

Ingestion

- 1-4 days
  - GI tract edema, ulcers
- 24-72 hours
  - Hepatocellular injury
  - Acute tubular necrosis
- 72-96 hours
  - Pulmonary fibrosis

Herbicides: Other

- Nitrophenolics: *DNOC Elgetol, Dinitrophenol, Dinocap, Dinoseb*

  -well absorbed dermally, orally and are quite volatile

  - local skin dermatitis, irritating to mucous membranes

  - irritation, nausea vomiting, dizziness, sweating, thirst

  Chronic Toxicity: maybe aplastic anemia or peripheral neuropathy (questionable). Clearly an animal carcinogen

  Persistent: Still contaminates some water wells in California

Herbicides: Other

- Glyphosate *(Roundup, Glyfonox)*
  - Very irritating to mucous membranes
  - Low toxicity orally
  - Not well absorbed dermally
- Triazines *(atrazine, simazine)*
  - Most are irritating
  - Low acute toxicity
  - May be associated with some cancers, endocrine disruption

Insecticides

- Cholinesterase-inhibitors
  - Organophosphates and n-methyl carbamates
- Pyrethrins and Pyrethroids
- New insecticides

Insecticides: ChE-Inhibitors

- Chlorpyrifos, diazinon, guthion, carbaryl methamidophos, aldicarb, malathion

  - Absorption: variable, but generally good in solution through all routes

  - Acute toxicity: variable but generally high many class II, some class I pesticides

  - Chronic Toxicity: neuropathy, CNS changes in severe cases

Insecticides: ChE-Inhibitors

- Signs and Symptoms
  - Nausea, vomiting, diarrhea
  - Weakness, twitching, paralysis
  - Visual blurriness, tearing
  - Confusion, lightheadedness, coma
  - Bronchial secretions, wheezing, edema
  - Sweating, salivation, urination

Insecticides: ChE-Inhibitors

Treatment:

- Atropine

  - antagonizes the effect of acetylcholine on receptors

  - used as a treatment for both OP poisoning and carbamate poisoning

Insecticides: ChE-Inhibitors

Treatment

- 2-PAM, Protopam
  - works by displacing the OP from the cholinesterase
  - used only as a treatment for OP poisoning NOT carbamate toxicity

Insecticides: ChE Inhibitors

Non-ChE effects of OP pesticides

- Odor health effects
- Irritant effects
- Organophosphate-induced delayed polyneuropathy (OPIDP)

Insecticides: Pyrethrins and Pyrethroids

- Pyrethrins
  - Natural insecticidal extract
  - Unstable
- Pyrethroids
  - Synthetic derivatives
  - Used with piperonyl butoxide

Insecticides: Pyrethrins

Pyrethrins

-Low systemic toxicity.

-In massive ingestion-seizures.

-Respiratory sensitization

-asthma

-Common symptoms:

- Paresthesia (burning numbness of lips and hands)

- Allergic dermatitis

Insecticides: Pyrethroids

- Use increasing
- Examples of use
  - Structural & agricultural
  - Pet flea control
  - Pediculicide
- Vector control
  - West Nile virus
  - Aircraft “disinsection”

Insecticides: Pyrethroids

Insecticides: Pyrethroids

West Nile Virus prevention spraying in North Carolina

West Nile Virus spraying in New York

Insecticides: Pyrethroids

- Health Effects

  Skin

  - Paresthesia, dermatitis

  Respiratory

  - Rhinitis

  Systemic

  - Dizziness, headache
  - Fasciculations, seizures,
  - Hormonal disruption *in vitro*

Insecticides: Pyrethroids

- Treatment
  - Decontamination
  - Vitamin E cream
  - Symptomatic therapy
  - Remove from further exposure if needed

New Pesticides Receptor Agonists

- Chloronicotinyls/Neonicotinoids: Admire®, Provado®, *imidacloprid*; Assail®, Rescate®, *acetamiprid*; Platinum®, Actara®, *thiamethoxam*; Calypso®, *thiacloprid*
- Phenylpyrazoles: *A broad spectrum neurotoxin that works as a GABA antagonist.* Fipronil®
- Oxidiazines: *Neurotoxic sodium channel blocker.* Avaunt®
- Pyrroles and Pyridazinone: *Uncouple Oxidative Phosphorylation*
  - *e.g. Pyridaben (Pyramite®)*

New Mechanisms of Actions for Insecticides

- Buprofezin: a chitin synthesis inhibitor (Applaud® Insect Growth Regulator)
- Methoxyfenozide: accelerate molting (Intrepid®)
- Pyriproxyfen: a juvenile hormone that suppresses embryogenesis (Various products such as Adams flea and tick spray® etc)
- Azadirachtin: From the Neem tree, (NEEMIX®, AZA-DIRECT®, ECOZIN®, AGRONEEM®) disrupts insect molting

New Mechanisms of Actions for Insecticides

- Spreading Disease Among Insects
  - ***Bacillus thuringiensis toxins***
  - **Paralyzes larval gut**
- Fungal Insecticides
  - **Causes fungemia and death**

Fumigants

- Wide mixture of poisons
- Most, acutely toxic to all life forms
- Most are acutely irritating
- Most are acute neurotoxins
- Most will cause shortness of breath, headache, dizziness and mucous membrane irritation

Fumigants

- Halogenated hydrocarbons
  - Methyl bromide
  - Ethylene dibromide, DBCP
- Inorganic compounds
  - Sulfuryl fluoride
- Pro-fumigants
  - Metam sodium
- Metal phosphides
  - Aluminum, Zinc, Magnesium

Fumigants: Methyl Bromide

- High vapor pressure
- Heavier than air
- Odorless
  - Chloropicrin added
- Toxic mechanism
  - Tissue methylation

Fumigants: Methyl Bromide

Acute Effects:

- Vesicant
  - Blistering dermatitis
- Lower respiratory toxicant
  - Delayed pulmonary edema
- Central nervous system depressant
  - Usual cause of death

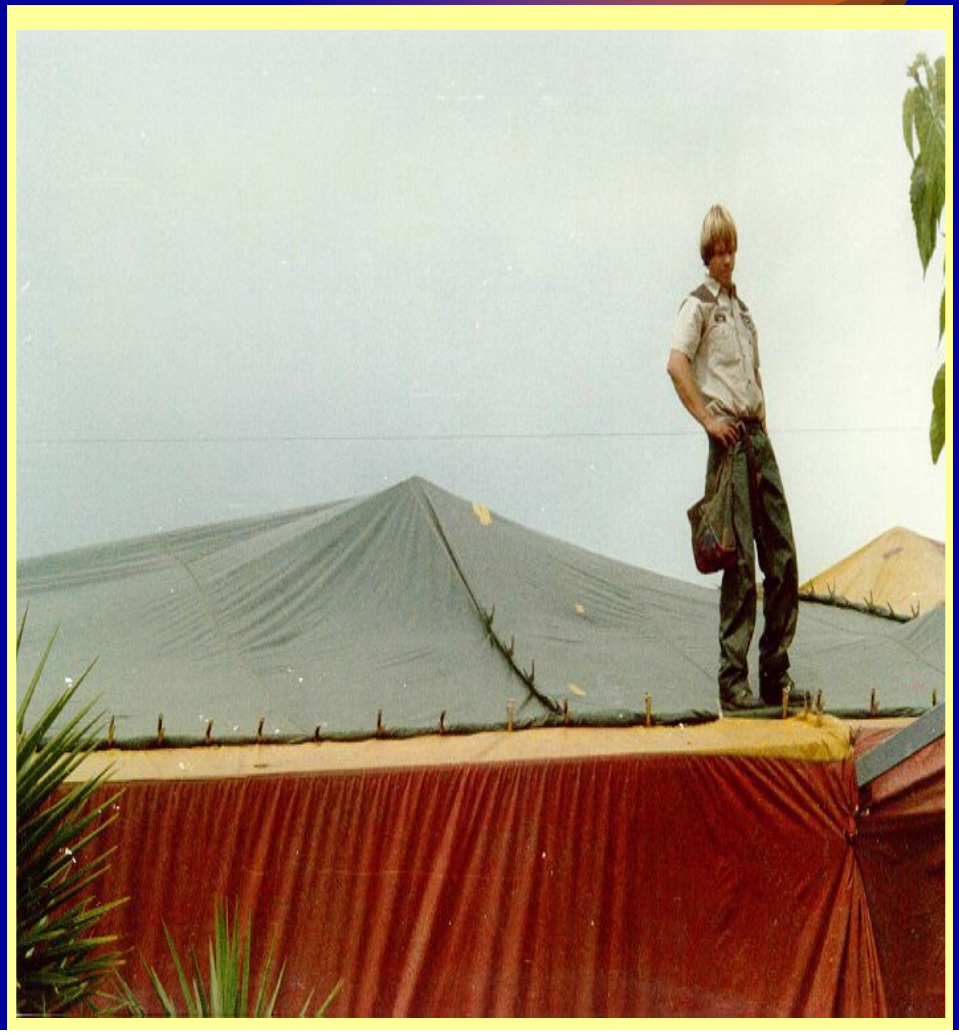
Fumigants: Methyl Bromide

Phase Out

- Ozone depletion
- Exemptions
  - Critical agricultural uses
  - Pre-shipment & quarantine
  - Emergency uses
- No “ideal” substitute

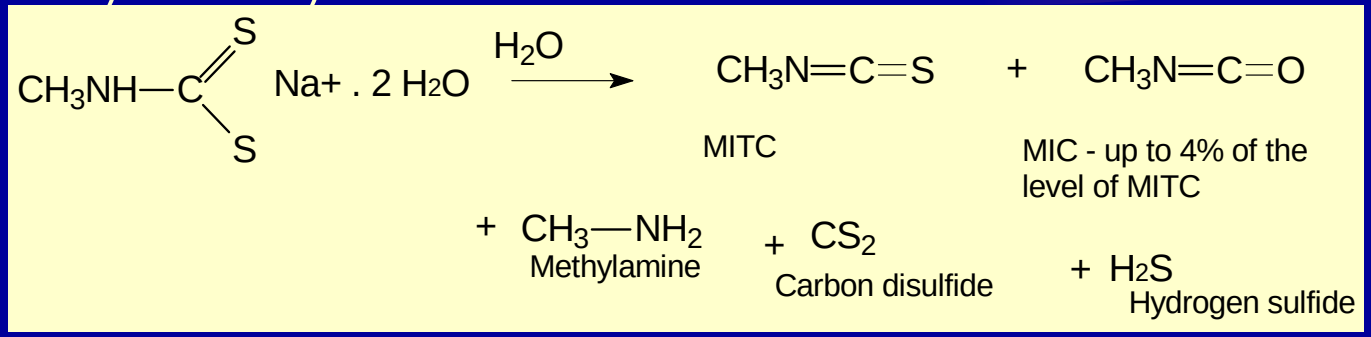
Fumigants: Sulfuryl Fluoride

- Pulmonary
  - Dyspnea, cough, delayed pulmonary edema, fatal hypoxia
- Renal
- CNS
  - Weakness, nausea, vomiting, restlessness, muscle twitching, seizures



Fumigants: Metam-sodium

- Hydrolyzes to mixture of irritants

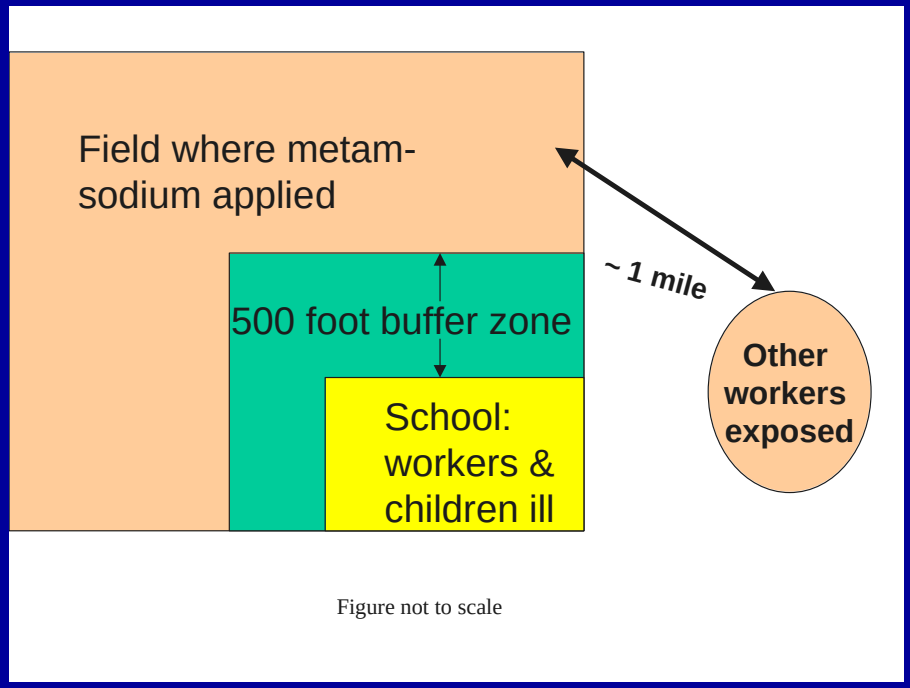


- Health effects
  - Irritant dermatitis
  - Reactive airways dysfunction syndrome/asthma

Fumigants: Metam-sodium

- Metam-sodium applied to carrot fields
- Illness reported among
  - School children
  - Workers

Fumigants: Metam-sodium



- MITC detected at school, beyond 500 foot buffer zone
- Workers required to monitor field for odor

Fumigants: Phosphide Compounds

- Metal phosphides hydrolyze
  - Aluminum, zinc, magnesium
- Phosphine
  - Colorless, fish/garlic odor
  - Highly explosive, corrosive
  - Rapidly oxidizes to phosphoric acid

Fumigants: Phosphine

Illness Syndromes

- May resemble viral syndromes
- Pulmonary toxicity
- CNS toxicity
- Multi-organ failure

Fumigants: Chloropicrin

- Characteristics
  - Colorless, slightly oily liquid with intense pungent odor
  - Heavier than air

Fumigants: Chloropicrin

- Now used as a fumigant (at 100% or in 33-50% combo with methyl bromide
  - Nematicide for soil
  - Insecticide for stored grain
- Currently used as a warning agent for other fumigants such as methyl bromide and sulfuryl fluoride
  - Causes lacrimation and mucous membrane irritation at relatively low concentrations

Fumigants: Chloropicrin

- Signs and Symptoms
  - Eyes: tearing
  - Pulmonary: Cough, shortness of breath, wheezing, pleuritic chest pain, bronchitis, pneumonia, pulmonary edema
  - Neurologic: headache, nausea, vomiting, vertigo, fatigue
  - Skin: Irritation

Fumigants: Chloropicrin

- Diagnosis:
  - History, Exposure history
  - Physical examination
- Management
  - No specific antidote
  - Treatment is supportive care
    - Decontamination procedures (flush eyes and skin)

Other Pesticides:Rodenticides

- Mostly anticoagulants
  - Generally very low acute toxicity
  - Not well absorbed except by mouth
  - Bleeding rare in humans
  - May be present in rodent feces and so persist after rodenticide is removed.

Other Pesticides: Disinfectants and Antimicrobials

- Sodium hypochlorite
- Isopropyl alcohol
- Gluteraldehyde, formaldehyde
- Quaternary ammonium compounds
- Other Mixtures

Other Pesticides: Disinfectants and Antimicrobials

- Acute
  - Asthma exacerbation, bronchitis
- Chronic:
  - RADS
- Treatment
  - Oxygen, bronchodilators

Other Pesticides: Propargite

- Omite™
  - Acaricide
- Contact dermatitis
- Sustained-release propargite
- Severe dermatitis with scarring

Other Pesticides: Deet

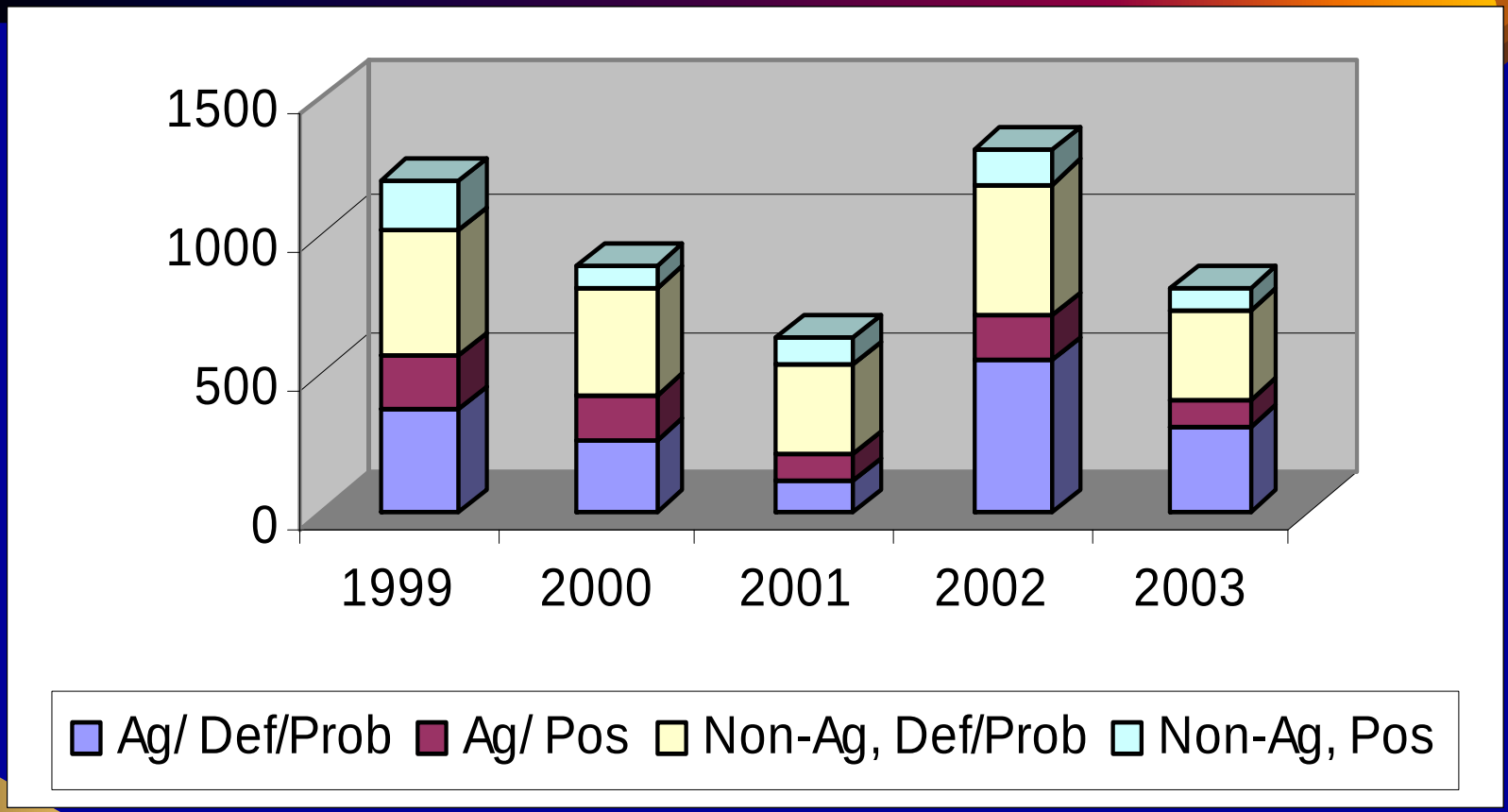
- Skin
  - Irritation
  - Contact urticaria
- CNS
  - Seizures, encephalopathy
    - Children < 5 years
    - High dose/concentrations

How Big is the Problem?

How many acute poisonings?

- **In US 10-20,000 per year**
- **World Wide 1-3 million illnesses and 200,000 deaths**
- **Counting all cases maybe 25 Million illnesses**
- **Studies show enormous underreporting world wide**

Pesticide Illnesses in California 1999-2003



Pesticide Illnesses in Sonoma County, 1999-2003